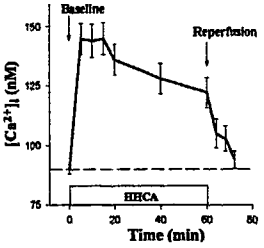
908-17 Hypothermic Hyperkalemic Cardioplegic Arrest Causes a Prolonged Increase in Intracellular Free CaLcium and Is Associated With Myocyte Contractile Dysfunction Following Reperfusion

Robert B. Hinton, Latha Hebbar, Jennifer D. Walker, Rupak Mukherjee, B. Hugh Dorman, Raymond C. Roy, Fred A. Crawford, Francis G. Spinale. *Medical University of South Carolina, Charleston SC*

Hypothermic hyperkalemic cardioplegic arrest (HHCA) is a commonly used technique of cardiac surgery. However, left ventricular (LV) pump dysfunction can occur following reperfusion and rewarming, the cellular basis for which remains unclear. We hypothesized that the prolonged membrane depolarization due to HHCA causes increased myocyte intracellular free calcium ($[Ca^{2+}]_i$), which is associated with alterations in contractile performance. Accordingly, time dependent changes in $[Ca^{2+}]_i$ were measured in porcine LV myocytes (n = 30) using calcium flourescence. Measurements were sequentially recorded in the same myocyte: during *Normothermia* (cell media, 15 min, 37º C), *HHCA* (crystalloid cardioplegia, 60 min, 12º C, 24 mEq K^+), and subsequent *Reperfusion* (cell media, 15 min, 37º C). In light of the fact that HHCA caused increased $[Ca^{2+}]_i$, we next examined myocyte shortening velocity at Normothermia (n = 268) and following HHCA and Reperfusion (n = 231) using video microscopy. Myocyte contractility following HHCA and Reperfusion was decreased compared to Normothermia (66.6 ± 2.1 vs. 33.6 ± 1.2, μm/s, $p < 0.05$).



Summary: This study demonstrated for the first time that HHCA causes a prolonged elevation in myocyte $[Ca^{2+}]_i$ which is associated with contractile dysfunction following reperfusion. Thus, fundamental mechanisms contributing to the transient LV pump dysfunction following HHCA include alterations in calcium homeostasis and myocyte contractile dysfunction.

908-18 Ischemically Preconditioned Myocardium Is Vulnerable to Reperfusion Induced Injury

Romas J. Kirvaitis, Irvin B. Krukenkamp, Ban-An Khaw, Paul G. Burns, Glenn R. Gaudette, Artiom Petrov, Aaron Goldfaden, Joshua Schulman, Sidney Levitsy. *New England Deaconess Hospital, Harvard Medical School, Boston, MA*

To adjudicate whether an impaired subpopulation of cells exists in preconditioned (PC) myocardium that may progress to irreversible injury during reperfusion, 36 adult sheep were evaluated at the end of 60 min of 37º C regional ischemia (diagonal occlusion) and after 90 and 180 min of reperfusion. Animals were randomized to PC (3–5 min diag occlusion) or control. Area at risk (AR) was delineated by monastryl blue pigment. Infarct size (IS) was determined by tetrazolium staining after 180 minutes of reperfusion. All other groups received an intracoronary injection of $^{111}InCl_3$-labeled antimyosin antibody and underwent gamma imaging for infarct delineation. LV to body and AR to LV weight ratios were constant. IS to AR ratios are tabulated:

Reperfusion:	None	90 min	180 min
Preconditioned	11 ± 7%*,#,†	21 ± 7%*	25 ± 4%*
Control	46 ± 19%	51 ± 17%	52 ± 10%

Data: Mean ± SD, *p < 0.05 vs. control, #p < 0.03 vs. pc-90 min, †p < 0.003 vs. pc-180 min; Stats: ANOVA, post hoc Tukey.

In contrast to the controls, infarct size significantly increased during reperfusion in preconditioned animals. This model suggests that preconditioning *does not* afford complete protection against reperfusion injury and opens the possibility of further therapeutic intervention to significantly limit infarct size progression.

908-19 Does Coronary Artery Bypass Surgery Cause Native Vessel Occlusion?

David Hair, Adrian Antonescu, Tetsuo Ishimori, T. Anthony Don Michael. *Central Cardiology Medical Clinic, Bakersfield, CA; University of California, Los Angeles, CA*

Previous observations have indicated increased progression of atherosclerosis in native bypassed coronary arteries. Consequently, we studied 119 arteries in 48 patients who had undergone bypass surgery and had second cardiac catheterizations for progression in 3 subsets with comparable times to progression. Arteries were divided into three groups: A) Nonbypassed native vessels; B) Moderately occluded (50–75%) bypassed arteries proximal to graft; C) Severely occluded (75–99%) bypassed arteries proximal to graft; D) Arteries distal to a graft. Comparable groups to A of nonbypassed vessels and to B and C of bypassed vessels were unavailable. Changes observed were classified into: 1) No change; 2) 50–75%; 3) 75–99% 4) 100% occlusion. In group D no major changes were seen. The mean age was 69.5 male and 68.1 female with 32 males and 16 females.

	A (N = 34)	B 9N = 26)	C (N = 59)
1	61.7% (Time = 61.7 months)	26.9% (40.4)	28.8% (63.1)
2	23.5% (63.9)	3.8% (12.0)	0.0%
3	11.7% (75.3)	42.3% (63.6)	8.5% (60.8)
4	2.9% (66.0)	26.9% (59.3)	62.7% (64.3)

Conclusions: 1) Native vessels (B, C) proximal to bypass grafts show significant disease progression, as compared with the changes seen in the *same* vessels distal to the graft. 2) Nonbypassed arteries showed much less progression of disease. 3) Changes in native bypassed arteries may have potential therapeutic implications.

908-20 Blood Pressure Response During Bypass Surgery in Patients Taking ACE Inhibitors

Carolyn M. Beale, Richard Underwood, J. Graeme Bennett, John Pepper, Christopher Lincoln, Peter Collins. *National Heart & Lung Institute, Imperial College of Science, Technology and Medicine, and Royal Brompton Hospital, London, UK*

Datasheets warn that patients on ACE-inhibitors (ACE-I) may suffer hypotension during surgery and anesthesia due to inhibition of angiotensin II production. This study investigated the response of systemic blood pressure (BP) to anesthesia and surgery in patients taking an ACE-I (quinapril (Q) 20 mg once daily) prior to CABG surgery. Sixty-five patients were randomized to receive Q or placebo for up to 6 weeks prior to surgery, in addition to existing antianginal therapy. Arterial blood pressure was monitored constantly throughout and following surgery. For analysis we documented the first 4 BP after induction of anesthesia (baseline), first 4 BP immediately after cessation of bypass (post-bypass), and first 4 hourly BP in ITU. The 4 recordings at each stage were then averaged (Table). Thirty patients received Q and 35 patients received placebo. The ischemic time was the same in both groups (mean = 56 min).

	Quinapril			Placebo		
	systolic	diastolic	mean	systolic	diastolic	mean
Baseline	110	68	79	112	70	79
Post-op	85	50	64	88	53	67
ITU 110*	60	77*	120	64	82	

*P < 0.05

There was no difference in BP between Q and placebo at baseline or immediately after bypass. However there was a significant difference between groups in systolic and mean BP in ITU (*, P < 0.05). Therefore Q does not cause hypotension during cardiac anesthesia and surgery, it maintains a lower BP in the immediate post-operative hours but does not result in the requirement of extra inotropic support.

908-21 VEGF-Induced Angiogenesis as an Alternate Method of Revascularization for Chronic Myocardial Ischemia: Improved Perfusion and Vascular Reactivity

Frank W. Sellke, Steven Y. Wang, Kazumasa Harada, John J. Lopez, Michael Simons. *Beth Israel Hospital, Boston MA*

Endothelium-dependent vascular relaxation and perfusion are impaired in the collateral-dependent myocardium. To examine the effects of the angiogenic agent vascular endothelial growth factor (VEGF) on these alterations, ameroid constrictors were placed on the proximal circumflex (LCx) coronary artery of pigs. In 6 animals, VEGF was administered extraluminally to the proximal LCx with an implanted slow-infusion pump. Controls (n = 6) were administered vehicle only. After 6–8 weeks the LCx was occluded in